Figure 1/10

gapmers

headmer

tailmer

mixmers

4-3-1-3-5

4-1-1-5-1-1-3

3-9-3-1

4-1-5-1-5

3-3-3-3-3-1

Figure 2/10

Figure 3/10

Figure 4/10

9 R=Ms, R^1=Bz
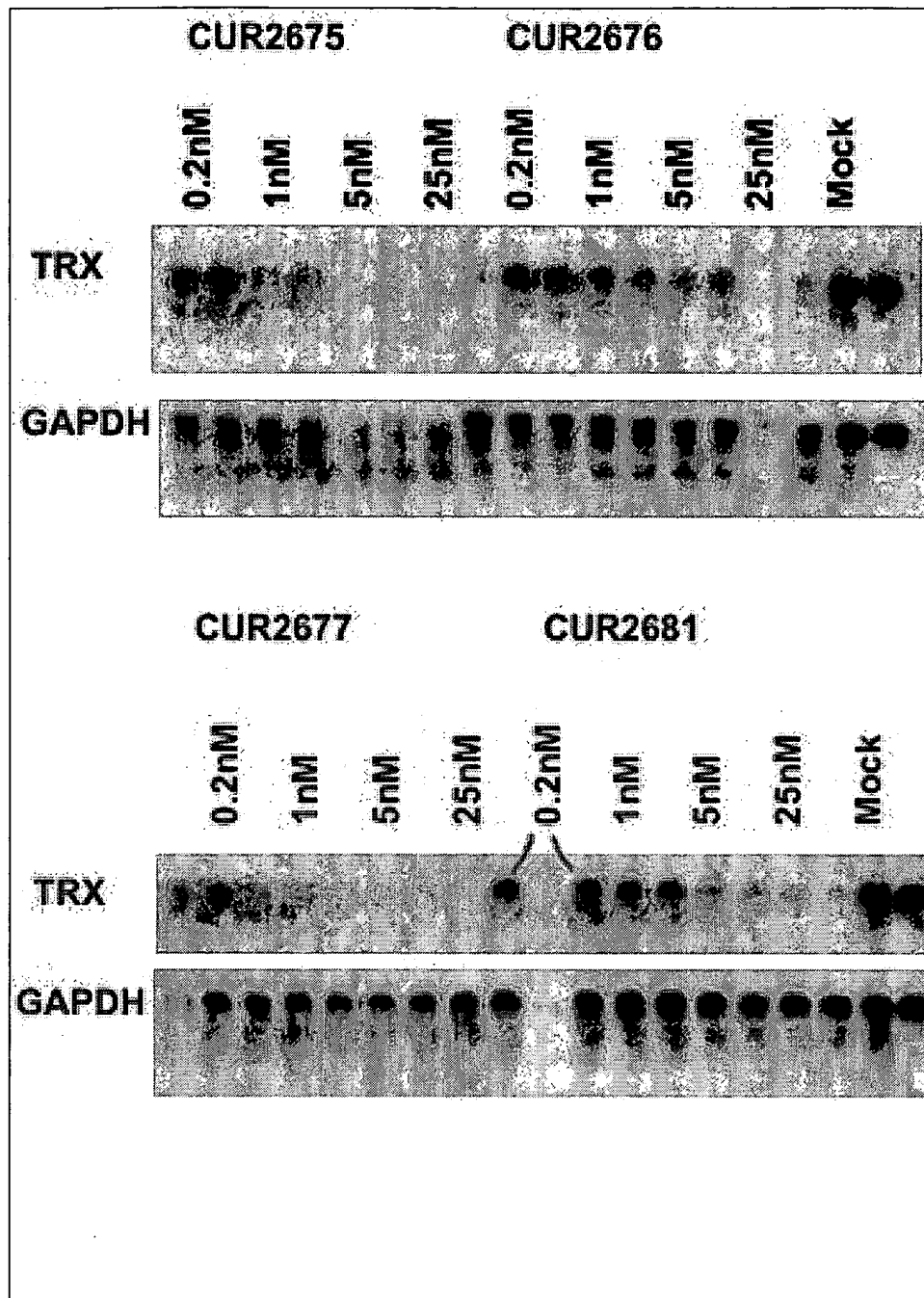10 R=R^1=Bz
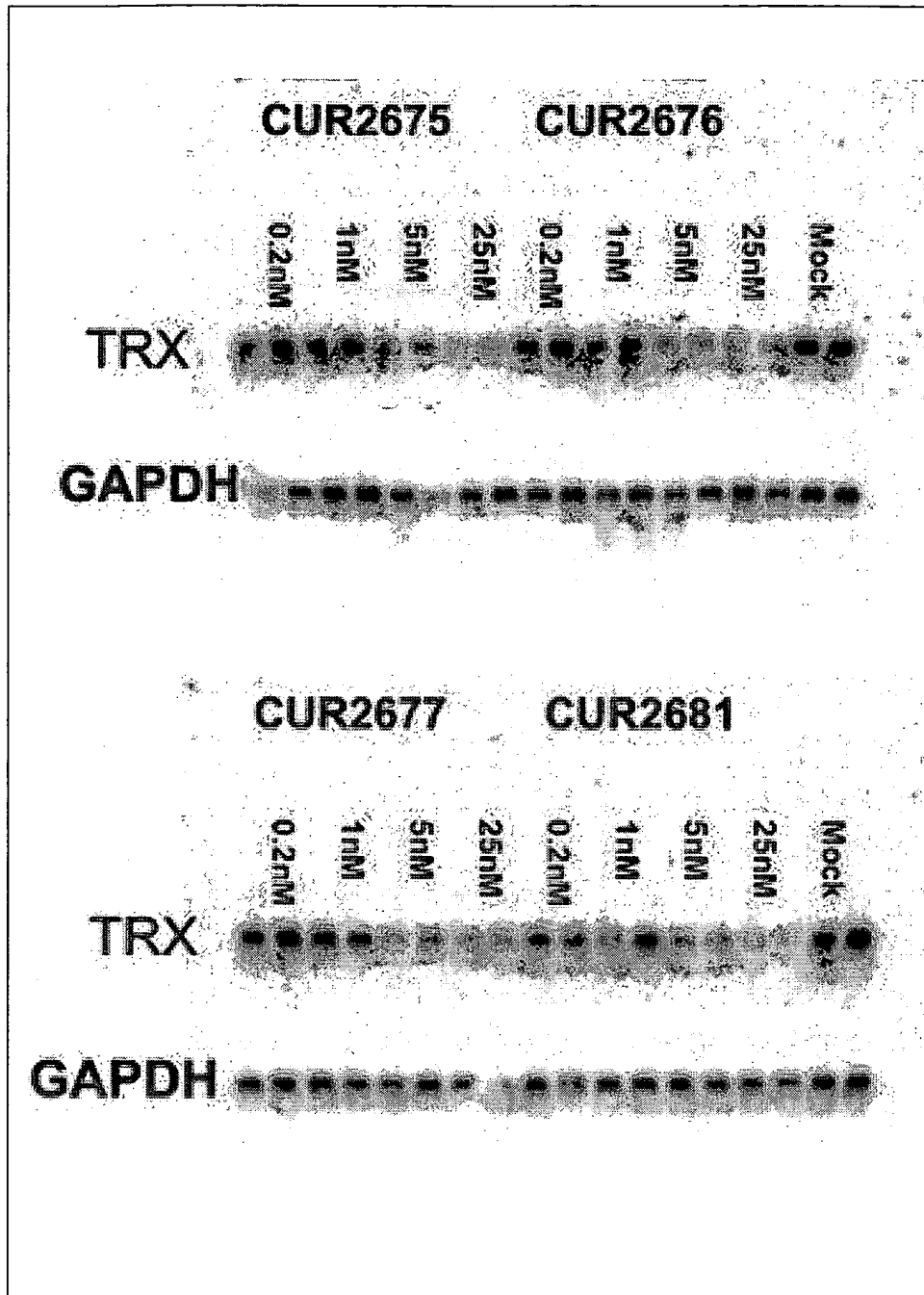11 R=R^1=OH
12 R=DMT, R^1=OH
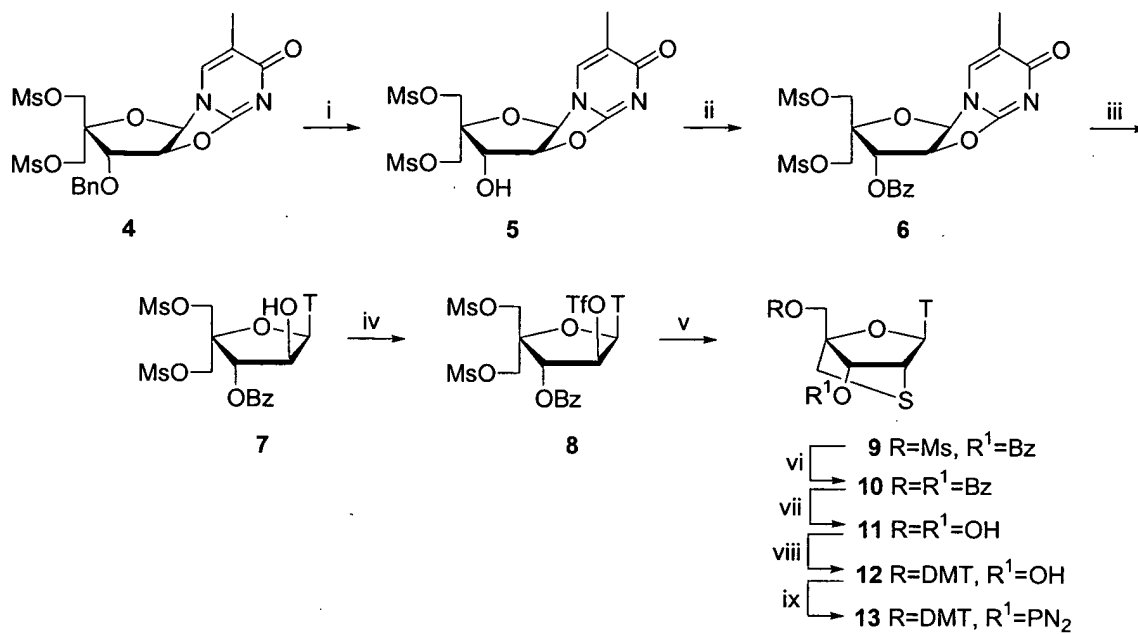13 R=DMT, R^1=PN$_2$

Figure 5/10

Seq ID NO: 1

BD132005

```
        agtcttgaag ctctgtttgg tgctttggat ccatttccat cggtccttac agccgctcgt
   61 cagactccag cagccaagat ggtgaagcag atcgagagca agactgcttt tcaggaagcc
  121 ttggacgctg caggtgataa acttgtagta gttgacttct cagccacgtg gtgtgggcct
  181 tgcaaaatga tcaagccttt ctttcattcc ctctctgaaa agtattccaa cgtgatattc
  241 cttgaagtag atgtggatga ctgtcaggat gttgcttcag agtgtgaagt caaatgcatg
  301 ccaacattcc agtttttaa gaagggacaa aaggtgggtg aattttctgg agccaataag
  361 gaaaagcttg aagccaccat taatgaatta gtctaatcat gtttctgaaa atataaccag
  421 ccattgagct atttaaaact tgtaattttt ttaatttaca aaaatataaa atatgaagac
  481 ataaacccag ttgccatctg cgtgacaata aaacattaat gctaacactt tttaaaaccg
  541 tctcatgtct gaatagcttt caaaataaat gtgaaatggt c
```

SEQ ID NO: 2

NM003329

```
        gaattcgctt tggatccatt ccatcggtc cttacagccg ctcgtcagac tccagcagcc
   61 aagatggtga agcagatcga gagcaagact gcttttcagg aagccttgga cgctgcaggt
  121 gataaacttg tagtagttga cttctcagcc acgtggtgtg ggccttgcaa aatgatcaac
  181 cctttctttc attccctctc tgaaaagtat tccaacgtga tattccttga agtagatgtg
  241 gatgactgtc aggatgttgc ttcagagtgt gaagtcaaat gcacgccaac attccagttt
  301 tttaagaagg acaaaaggt gggtgaattt tctggagcca ataaggaaaa gcttgaagcc
  361 accattaatg aattagtcta atcatgtttt ctgaaaacat aaccagccat tggctattta
  421 aacttgtatt tttttattta caaaatataa atatgaagac ataaccagtt gccatctgcg
  481 tgacaataaa cattatgcta a
```

SEQ ID NO: 3

D28376

```
        gccgggcgtg ccagtttata aagggagaga gcaagcagcg agtcttgaag ctctgtttgg
   61 tgctttggat catttccatc ggtccttaca gccgctcgtc agactccagc agccaagatg
  121 gtg
```

SEQ ID NO: 4

AF 548001

```
    1 gttatagatt ctgctctggg tgctccatac agctccttcc tctctgcccc aataacctcc
   61 ctctctttgg gaacattgct gcattcaggg cagtctgtct tccctcccta tgggctgtct
```

121 ttagaatgtg tcccttgcct atatccatat tcatgctccg tgctcctcag cccctagaa

181 actttgcaca atagattcaa aacctctggt ttcctccctt cctctgtctg aaagagtgaa

241 agaaggaagc cagggatttc aggggggcagc caggcagcag tatcaccacc cctaggcaat

301 cacacctagt tgcagcttca tcgggaacag ctcagctctg aaaacacaga cctgggactc

361 tccctcccag ccttctagct ctcgttcctg tgagcagctt ttcaacctcc acttccagcc

421 gctgacaggc cctcctggct ccacaaggcc agctaacata cccaccttcc acaatcccca

481 gccctgccag acataacctg caacaggcat tcctggatca atgcaaactc cgacttctgt

541 tccaggagtc tgcctctgtt agaagaatct cacacaagtg tgcgtgctgt gccattgtaa

601 atgctgtata aggtggccag gcccaatcag tccctgcaag acaccgaaca gtaagaacta

661 tctatggagt gtttactatg tgccaagcac cgtcctttgc aagcactatt aaccctcaaa

721 ataccaccac cgtgagattg agaccatcat gattcccgtt ctacagaagg aaacactgag

781 actttaggag gtcaggacct ttccagggtc acaactgcgt aactaagttg cagagctcaa

841 cccagtggca cttccatctc acacgcagct gtctgatggt caagagccca accagtcccc

901 cggtcgtttc taccgcacta aaccgctgtg tcaagctgga gcagcgggct cagcagtgaa

961 aatgaaagaa cagaaggagg ttacagagaa gagaacggtc acggtaaatt ccggagagga

1021 ggcaaggacg tacacaccga gatacttccc ggtcaccgtt actcagcact ttgtgggggtt

1081 cacgtggctg gggggggccgg ggcgtggcgg ccctttttcga ggaatccagc cctgcctggg

1141 cggtcccccat ctcgagcgtg ggcgtgttcg attcaggccc ggcggacgca tccccaggtg

1201 acccgggagg gaccttgtgt ctctgggggt gactgtccgt ctccccgcct cccaccgtca

1261 cgcgcagtgc tgatccccac ttccagctgg tgtgcgagct gggcttgggg gtacaggagc

1321 tgaagccctg gagctccgcc ccacgcttgc gccagccccg ccccgatccc ggctcgcagg

1381 ctccaggggc ggggcgtggc cggggcgcag cgacgggcgc ggaggtccgg ccgggcgcgc

1441 gcgccccgc cacacgcacg ccgggcgtgc cagtttataa agggagagag caagcagcga

1501 gtcttgaagc tctgtttggt gctttggatc catttccatc ggtccttaca gccgctcgtc

1561 agactccagc agccaagatg gtgaagcaga tcgagagcaa ggtacgcgct accggggaag

1621 gccagggtgc cggcgccgcg cgcggcctct gtaactgggg aaggcggtgg cgggaggtgg

1681 ggaaggcggt ggcgggaggt gcggaggccg cccctccgca tcgccagggg aaagggacgc

1741 ggcgtctcgg cctgggactg cgggaagcag cggcctgggc gcgcccgagg cggtggagcc

1801 tgccctggag gaagggagga gaaggacgag ggtcccctgg agggcggagt ggcggtgccc

1861 agcgtttctc gcaccctgtt cctcgggggga ttgcacgcac gcggggagcg tccggggggat

1921 gtgagagcgc agacagcgtg aggagtcccc acgctgcgcc tcctgcaccc tcccgtccgg

1981 gcagccccga ctggaggaag atgagggaat ggaaggggtc cgcccttggc cccccatctg

2041 tatccagatt caggccccag gcaaggatag ggagggccct tgcagaaggc acgggtcggt

2101 ggccgccgct gcctttccgt atgtgaagtg atccacccgc agcgggggta gtgatctccc

2161 tttgggagcg ggtctaggcc ggagaccccc gcctgcctcc acccatgccc gaccccaaag

2221 gtgacgcgtg ctgtatccgc actaaggggg cggattgcgg ctggagaccc cctggcacgt

2281 gcaggtctgt ccaggaggcc cgagggcccc aggtgaccgc gaggaagtga ggtccgggcc

2341 gcgcccacgg gactcctgtg gcgcagggcg cgtttccggc agcagtggct ttggaatgac

2401 tgagtcccca aggttgggcc cgggggcctc ggctgccctg cccgtccatg attcaccctc

2461 agtcggtggg ttttgctgga gccagggttc ctcctgggag cagccgcgcc ctgctgcctg

2521 ctcgccgacc tatcggtatc ccgatcgttg ttttgtcctc ttaaaaatgc ccaaggcgaa

2581 acagccttcc catgtttgaa agttattgca agcctaaaac cttgtagact gggaaaccca

2641 gagcctaacg cgcagtgtct agtccaatgt agccactcca gaaatatttg ttaaatgcag

2701 cgtcagaaaa gtgagtggag gaaattgata ctgctcgaac ggtagaagac ccctcgccag

2761 cgcctaccct gcgattaccc ctccctacct gcgggaagca gaggagggcg ggtcctcgcc

2821 cgcctcgggt gccctgacct gtttggtgcc gggtgggctt cggaaacaga agtgtgtctg

2881 caatgtgtcc ccgatccttt tgttcctttg attattattg actctcagtg ttttttcctc

2941 atatgttgat tgccactgtc atctttatc ttcctctcaa tcagtttttt cttagtggga

3001 ttctcatttt agcagccctc atgtgttgaa aagatcctta gtagtgaatt gtctttcata

3061 tacttttttt ccaagcacct attgtgtgac aaattattaa tccattcctg gggaagggag

3121 tggggctggg attctgttct ccagggtctg gcaacctcag tataacccaa ctgctaagaa

3181 ccccctccac tgagccagaa gacctttgag tggtctatgt tagttgtccc aaaatccaga

3241 cactacaaac aaagttgatt aggatttctg gagcacacag tttagtcctc ccagttgtca

3301 gagcatgtca gagcaccttc ctcctctacc agtgacaaag gtgtacaagg gtgacaggaa

3361 ctttaaaaaa agcactacag cctgggggccc aaaggccctg ataatcaatt aatcctcaaa

3421 ataacaatcc aaagtcattg atcgaaagtt acactaattt gattgttatt tgtctgttag

3481 tttgtttttc gagatggagt tttgcccttg ttgccctggc tggagtacag tggcgcgatc

3541 tcggcccact gcaacctcca cctcctgagt tcaagcgatt ctcttgcctc agcctcctgc

3601 acagctggga ttacaggcat gcgctgccaa aatgcccagt aattttgtat ttttagtaga

3661 gatggggttt caccatgttg gtcaggtttg tctcgaactc ctgacttcag gtgatccacc

3721 aacctcaggc tcccaaagtg ctaggattac aggcgtgaac caccacgccc agcctgttat

3781 ttgtaaatgt tgaatacatg ttacattttc atcctaatgg gctaaatttg caccatttgc

3841 cattcagaac aattctgttt ctgaggtact ctgttggtgc tttagggcca actgggatct

3901 atttcagaga ggaatggaat aattgactgt aaatgtgatg aggaagaaat aaacactttt

3961 aaaaaaaatg acacctacca tttattgaac tcccatctac aaggcacttg gctaagtact

4021 tcagaaacca ctcacactta ttaccctcag agtaggtatg ttgaggcaac gagatcttag

4081 actcttgctc ctatttaccc caactacact gttctgcttc ccccagatta ttggtgtcag

4141 tgatggagac atttattaat cctgttagtt tctgggagct agaaattgtg atttcttctt

4201 agtaatacaa tcttgaataa ttttcaagct gatacccgtt tagaagtatc agaagagaat

4261 ttgtacatga agcctgcaca tacgtggggt gtaactcatg ttcagttagg ctaaaagtta

4321 ttgttgcgtg cctcttttca gaattttagg tacttgtgct taaatttgat tcagaactgt

4381 tttggaaaag ccttgagtat gtttgaaata ccttccctct tgaaagtaat ctcaagtttt

4441 taataagggt taatcatgtt aaaaaaacaa aaatgtctat tcaaccagac attggcattt

4501 cttgaccttt tttcctgtct tacctggatc ttgcaataaa ggatgcctgg tttaactttc

4561 ttgaaaatca cattagggaa ggctttgaat gaaattgatc tggaacaata agtgatgatt

4621 tggaaaaaca attgctatac ttctatgtac cctgctgcag ctctccccat gtctccacct

4681 ctagaggtgg ggttcaggga tttgcataac taaaaaattt atgaaagtgt tgtcctacct

4741 ttctcaggaa caccatttgt gaattatttt cccaaaaacg aggtagaaat tagaaatcta

4801 gagaagtaac tattagtaca tgaggtcata ttagtgtttt cttgttgggt tttttttgt

4861 ttatttggtt ttttatctta tggttttta tttatttgat ttctttcttt acgagacctc

4921 ttgtggcggt ggggggcggg gaatgttcat tttttttaa acctatttga ccagcattgt

4981 ttccttgaag aaaacctaga tttcagatac agatgtttat gttttgattt atcttaattg

5041 ctctggtttg gtttttgggt ttggtcagca ctaacgtact aatgtggtta aaatgagtcc

5101 tttgttttgg gaggccaagg cgggtggatc acttcaggtc aggagttcaa gaccagcctg

5161 gtcaacatgg cgaaactctg tctctactaa aaatacaaaa attagctggg actggtggca

5221 gaggcttgta atcccagcta ctcaggaggc tgaggcaaga gaatcacttg aacccggag

5281 gcaaaggtta ctgtgagccg agatcaggcc tttgcactcc agcctgggca acaagtgaaa

5341 ctccgtctca aaacaaaac aaaacaaaaa tgagtccttg gtaactagaa tattcggttc

5401 ccagggttac agtatctaga tagtaaataa ttcagggaag ttagtggtaa gagatttctt

5461 gatcatttct actgagaatt ttatttaaca agcattcctt atgaaaaata atatctatga

5521 aaaatttcct tcatgaggaa cgaaaacttt catttaatga atgacaaggg tatagtttta

5581 aaataaaggg caaaaatcaa aggttggtaa acgtgtgatc tcagctctgg aaaccccatt

5641 atgcttatgt caacggtgat gtctgagtgt tgaggtttgg gaaaggtgag tttccttgac

5701 ttttcaaaaa attttagatt ttcgtatggt ccaccataga caaatgagtt taatcaaaag

5761 tcatagcttt ttttttttt ttttttttg cgacagagtc tccgtctatt gcccaggatg

5821 gagtgcagtg gcacaatttt ggctcactgc aacctccgcc tcctgagttc aagctattct

5881 cctgcctcag cctcctgagt ggctgggact acaggcatat gccaccacgc ccagctagtt

5941 tctgtatttt tagtagagac agcatttcac catattggcc aggctggtct cgaactcctg

6001 acctagtgat ccgcccacct cggcctccca aagtgctgag attacaggtg tgagccacca

6061 tgcccagcca acttttatct ttaagtaact tgtgatgttt caattgcaaa atcctatgcc

6121 tttgtgactt caagtgaccc ctttcataat ccataagtgt ttaatgaatg tctaccatat

6181 acctagcctt gacatggaaa cattttaat acaaatgtct atttttattt tccttttgtt

6241 tggtgtagag aaaaaatagc cagttcacaa tattttataa aatagttatg aagagaatgt

6301 cagtatactc tacacatatc ttgtttcatc ttatcaagta acactaccaa caatgtatag

6361 aatttcttca aactgagttt tatttggctt gtttggggat tttttttttt tttttttttt

6421 tttttggct aaaaagtagg tcctgaaagg aggacctcca gaatgtgctt tgtgtcattg

6481 tgtcgagtct ttcttttgaa ggtttaatat ttaactattt atttaatata agcttttctt

6541 ttgctgttag actgcttttc aggaagcctt ggacgctgca ggtgataaac ttgtagtagt

6601 tgacttctca gccacgtggt gtgggccttg caaaatgatc aagcctttct ttcatgtgag

6661 tattaaacaa tgtctgcttt gtaagagatt tgtgtttttt gagttggtgg tcacagtggt

6721 aggaaagaaa gacagttaaa ggattttggt ttcggtgggg ggatttcttt ggctggatct

6781 ttggtctaaa agtagtagta taacaaataa tttaggtttg atacatgtag cccattgaaa

6841 acaaattta gaagttaatt ttgtcttaaa tagttctttt tttccccaca ttgaaacatg

6901 ggccttattt gaaatcccag cctcagaatt tgatatgcca agctgtttta tactaagaaa

6961 aatttgattt agagaaaatt tatgtctctt agatctatgt ctccaaagat ctaaattttt

7021 ggatctttaa ttagtctcta cttttattaa gtttccattt aagaagcttg ggtatgttga

7081 ttgccattac ctagttctaa atctttttgg atttttcatt ttaaattttc cagtccctct

7141 ctgaaaagta ttccaacgtg atattccttg aagtagatgt ggatgactgt caggtatgta

7201 gctggaaata tgagatactg ctgagctttt cacattggcc tttttctctg aattgcacag

7261 tgctttttc cataaatatg tcaaataatt ctagaactgt aatcctatct aaaaagttct

7321 atctcagaag agcaggcaag ttaggagctt aatcctagct atcgggagct gtatatcaca

7381 tcctaaagta aacaaaaata aatgagtgag acttctgaat cttatcggcc acccacctt

7441 ctaaaaccct acattctact ttacactctg agatgtgcaa taaatggaga ttgaatttag

7501 ctatgatcat tacatccata ggcttgatgg agtcaccaaa ttatgagacc gcttgtaggg

7561 ctctttgtga acttgcagta gcatgagaac ctgcatttgc aagcctattc tagtcttggt

7621 tgattttagt caattagaaa ccacaaatgt tttaacaaat aaacaccaag gtacctgaga

7681 gaataatttg gaagaaattc caggggttggt tgtatttaac aaatacttgt tttgcactag

7741 gtatatacca ggcactgttc tgggtggttt ttaagtatca gttcatttaa tcctgagtgc

7801 tgttatcatc cccattttat agatgagaaa actgaaacac agaggttgtt catgaagttt

7861 cagtgagtat gtggctgaac taggatttaa aatgaagtgg tctggcttcc cagcccttga

7921 ccttaagcac tacccatcgg aggatgctct gtcttgtggg tgtagatcgg gtgcttagca

7981 catgaccaca gacctaggag agcgggttga ggaggtatca cttcgggggcc ctttacagat

8041 atgtgagcat tttcacttag ccctagtgga gaaggaaagg cgatggggga agggtgcagt

8101 gtggcaacag aggcgctgga cctggcttcc agtcctggct cactagcatc tgcttaggcc

8161 agtcactcct cttccttgag ccttaagacc tgccccatca acctcccaag gttgcttatt

8221 cattgagcaa acatggaata tccaataaag ggtgaagggt cacttaaaac aggcatatgg

8281 cagtgctctc taaacatggg agggcgcaac aaccccagat tgtgtattct tagccagttt

8341 ttgactctgt gccttgggca acccctgcct tggcttgtgc tgtcttctcc atctggcctg

8401 tcctttcctt tcctacctga ctaactcctt gtcatgagct tcaccccttc tccacttacc

8461 gccttgtgtg ccctaagtac ccagtgaatc ttggcaatta ttataatgat ctttatgtct

8521 gtcctttacc attagtctca gtagattcct aggatcagag accctgtctt aattcacgtt

8581 ggttgcccct tcacctagca cacctgcctt gcatgtagta taggtgtgga atgaatgaat

8641 gatgaatgtg atatggttgt taagttacta ttctagatgt gtcccagagt tgtttttttt

8701 ttttaaaaa gagtgtaatt gcatttttgt gaaaaatcct tatcccttgt tttaatcaaa

8761 cttagtctta ttaaggtcaa tttagctagg ggaaaattgc acctggaata gagaaattct

8821 aactgccact gatcctatca gatagcaact tgatttttt tttttttttt tttttttttt

8881 ttttttgag atggagttca ctctgtcacc tggggtggag tgcagtggca tgatctcggc

8941 tcactgcaac ctctgcctcc cgggtttaag caatcctctg tcctcagcct cctgggtagc

9001 tgggattaca ggcatgcacc accatgcctg gctaattttg tatttttaca aaattaaaac

9061 cccagtagag acggggtttc accatgttgg tcaggctggt ctcgaactcc tgacttcagg

9121 tgatccaccc acctcggcct cccaaagtgc tgggattatc caccacgccc ggccttgatt

9181 tttatttgaa agcaataata ggtgccagat gccatgataa gccctttgca tgcactatgt

9241 catttaatcc tcacgataac tatacgagta ttttttatta gcaccctcat tgaacaggta

9301 atggcactgc agcacagaag gtaaagtcag tctcttgagg cagaccaatg caccatactg

9361 tactgaggac aggtcttctt actgccttta ggaagtacag tcatgcatca cttaatgatg

9421 aggatacttt ctgagaaatg ttaggcaatt ttgttgtgca cacatagagt gtacttacac

9481 aacctagatg gcatagcctc ctgtacacct aggctatgtg gtaaagcctg ttgctcctag

9541 gccacaaaca ggtaaggcat gttactgtac tgaatactgt aggcagttat aacacaacag

9601 taagtatttg tgtatctaaa catagaaaag gtatggtgaa aacatgatat gaaagattaa

9661 aaaatggtat gcctttataa ggtacttgcc ataaacggga cttgcaggac tgagaggtgc

9721 tctgggcgag tcagtgagtg ggtggtgagt gaatgtgaag gcctagaacc tgtagacgtt

9781 ataaacactg tatgcttaca aattttattt ttaaaatttc ttttttcagc aataaattta

9841 ttgtaacttt tttactttat agttttttta ttttttttaac tctttaactc ttgtaataac

9901 acttagctta aaacacgaat gcattgtaca gctctacaaa aatattttct ttatatcctt

9961 agtctataag cttttttttaa aaagactttt taaacttttt gttacaaact aagattcaaa

10021 cacatacatt agcctagacc aacacagggt caggatcatc agtatcactg tctcccatcc

10081 ccacatcttg tctcacagaa aggtcttcag ggacagtaac atgcatggac ctttcatctc

10141 ctatgataac agtgccttct cctggaatgc ttcctgaagg gcctgcctga gcctgttgta

10201 tagtaactgt ctttttaaaa aaataagtag gagtacactc taaattaata atgaaattaa

10261 agtaaataca aaaaccagta acgtgggtgt ttattatcaa gtagtatata ctgtccataa

10321 ttgtagtgat atgctttttt aagtgaaagc aagtttatta agaaagtaaa ggaacaaaag

10381 aatggctatt ccgcaggtaa agcagtctgt agtggtatac tttgtatgta attgcagcgc

10441 agatttgttt gcaccagcta atgcgatggg ctatgacatt aacccatcac taggtgagag

10501 gaatttttca acttcattat aatcttatgg gaccaccaca tatatgcaat ctgttgtcga

10561 tctaaatgtt atatggtgca ttactatagg tgtgcaaagc actcgaggac ttccgtatga

10621 cagagctcct ccttcatgtc tgcttggtgc accctgatca ccctgaatgt atcttttttt

10681 tttttttttt tgagacagag tctcactctg tcacccaggc tggagtgcag tggtaccatc

10741 tctgctcact gcaacctcca cctcccgggt tcaagcgatt cttctgcctc agcctcctga

10801 gtagctggga ctacaggcag ccgctaccac accaggctaa atttcaactt tttagtagag

10861 acagcatttt gccatgttgg ccaggctggt ctcgaactcc tcacctcaag tgatccaccc

10921 gtcttggcct cccaaagtgc tgggattaga ggcatgagct accgtgcctg gcctgaaagt

10981 gtcttttaaa accttgaagt gaccctctga caaactgagg aactttaact ttgcctccat

11041 agattgatag aaaagtatga gtagtagccc ttttgaaaat gatagaccaa ccttatttct

11101 ctgacagcca acagggttat gatacttatt ttataaatgg taacctccct ctgacccatta

11161 cttggagtga gttttcaata gtatgcattc aataaacatt caccattttt attccagcca

11221 ttactgtcct tgtgcctctt actggaacct gtactttcat gctcagcagg tgtccagcat

11281 taaaagaaaa agtaaagatt acctagaaag aactcctcaa cagtagtgcc acccaccatc

11341 ctagaggtcg tcatagtgtt tgtagctggc ctttcttccc cttgagaatt ctccgttggt

11401 ttccgtgatt tggttatcaa cagtcctgcc tgctcgcttg ctgtcctgtg tagcttttgc

11461 tgcttaggtg ctgagtggtt ctatatttct ttcccagtcc tcttttgagt gcctggctga

11521 cattttcaat ctctattggg ctccaaacca aaccagtttc gtggtattgt cctccaaacc

11581 ttgccctctt atagcatgaa caatgtgttg agcatggggt attataagag ttctcattta

11641 gcattccaca gttgaggaat gtgtgttact tcaattacct ttgagctgta gaaaaatctt

11701 tagctgtggt aacagccact tctaggagag gagaaaatac ggatcaacta gcccaatttg

11761 cgatgttagg aatttgtcga ttttcttagt aggatggctt tcaaaggtta gagcatcaga

11821 gtcacctgaa gcccgacttt aactgtaatg gtttaagatg gggttgatgg ggaaacttgt

11881 agtacccctc aggtaattct gatactgcag caaggtttga gaattcacaa agtctttta

11941 tttttcctcc cgagatagtc tcattctgtc gcccaggctg gaatacagtg gcatgatctc

12001 agctcactgc aacctccgcc tcccaggttc aagcaattgt cctgtctcaa cctcctgagt

12061 agctgggatg acagatgtgt gccaccacac ctggctaatt tttgtatttt tagtagagat

12121 ggggtttctc cgtgttagcc aggctagtct cgaactcctg acctcaggtg acccaccggc

12181 cttggcctca caaatcagtt tttaattaaa aataagcagg aggctgagtg tggtggctca

12241 cacctgtaat cctagcactt tgggagcccg aggaaggtgg atcacttgag ctcatgagtt

12301 tgagaccagc ctgggcaaca tggagagacc ttgtccctat aaaaaaaaaa aaaaaaaaat

12361 atatatatat atatatatat atatatatat atatagtgtg tgtgtgtgtg tatatatata

12421 cacacacaca cacaaaatta gccaggtgtg gtggcgtgtg cctgtagtcc cagctactgg

12481 ggaggctgag gagggaggat ggcttgagtc tgggaagtgg agattgcagt gagctgagac

12541 tatgcccctg cattccatcc agcctgggtg acacagccag accctgtctc aaaaataata

12601 ataatcagta aacccagtgt ggggttattc ctttagatta ctattatttt gttcttgaac

12661 aattgatttt tatttttta gacttttag cctttatata atcattctgt gtactctgcc

12721 ttcataataa aactggaaaa attatgagca agaaataaga ggtactagtt ctgaggaata

12781 gttaagatta tcatactgag tccaattgta gcagaatttt ttgttgcttc tttgtatgat

12841 acttaaaata gttgaaaatt tgattggatt aaagagcata ttggatcgct ggagtatctg

12901 atgctagtaa cattctgaac attctgcctg ttaatgtgcc cgtcaaagga agtaaatatt

12961 aataaaactt cttcattgag aatataaccg gtttggcttt tgtactgcca ttatattcat

13021 tatattaatt ttcatatgct gaaaaatgtc ctcatgcgga aatgtggggt acatgacagg

13081 gaaaagtttc tggttttgga ttacttctgt caaagctcag tactcgcagt cttgtattta

13141 atcctctccc tttgctactt tccctaccag gatgttgctt cagagtgtga agtcaaatgc

13201 atgccaacat tccagttttt taagaaggga caaaaggtac gtacatctga cctttaaaac

13261 tctaacttct aactgggcaa taggaaaccc agtataagtg aataaatcac tggagtgatg

13321 ttccctttaa agattgaggc atatcaccaa gttctgcttt taagaatttt taaatatgcc

13381 aaaattcatt ggcttaagta cataatgtga cagctaactg aaaatcaatc tttcctagaa

13441 ctagtcctat ttatatcata aagcacatag aatttcttag acttgggcag ttcatttgtt

13501 gttaagtatt gtgtaaaaga aaatttgtac ttgagccttt tgacttttct cttgatattt

13561 tttctttgtt tataacttaa atgaactgta tgttattcag ggaagtttat tttaaataag

13621 attatacttc tttttccctc cacccctatt cttccttcat tctatgctga atacatattt

13681 atacatatgt atatatatac atatgtatat gtatatatat aaatacatat ttatacatat

13741 tttatgtata aaacagtgct acagtgctac gtctaatgtc aattcaatat tctcttaaca

13801 ggtgggtgaa ttttctggag ccaataagga aaagcttgaa gccaccatta atgaattagt

13861 ctaatcatgt tttctgaaaa cataaccagc cattggctat ttaaaacttg taattttttt

13921 aatttacaaa aatataaaat atgaagacat aaacccagtt gccatctgcg tgacaataaa

13981 acattaatgc taacactttt taaaaccgtc tcgtgtctga atagctttca aaataaatgt

14041 gaaatggtca tttaatgtat tttcctatat tctcaatcac tttttagtaa ccttgtaggc

14101 cactgattat tttaagattt taaaaattat tattgctacc ttaatgtatt gctacaaaaa

14161 tctcttgttg ggggcaatgc aggtaataaa gtagtatgtt gttatttgtt atcttttgac

14221 agagaaaata gcattctctg ttttagcagg tgaatcctct atgctctcca aaagatcagc

14281 atgaccaaaa ttgatgtcca ctcatgaagg acttgttcgt tttgtttgtt tgttttgcca

14341 cgaggatcgg atcttgattc tcctcgaagt atctgagaaa gtctagttgt ataggccaga

14401 cataggttct gtcttgagtg gtaaaagttg tgggaaatta ttacttatat cattcaaaga

14461 acattgtttc ttgtgttcta agcacagtaa ggggttgggg gtttgaagaa actttttgag

14521 tttacataat aatgaagagc agaattatca tatgccaggt atcatctttc tattaattca

14581 cttaatcttt gtaacaatcc tattagatat agacactata atccccattt acctgtgagg

14641 aaacagacaa agggtggtaa tttccccagc atcacaacta gtcattggag gagctgggat

14701 ttgaaccaaa gaagtctggt accagaatat gtgcctttaa ctactacatt gccctcagtg

14761 caacaatctg agtaagcagg aaaatgatgg gcccttagtt gagtttcttt cctcatgtga

14821 aattaggatg ccaaacttag atgatctctc aaaatactaa tggaatgcct gttatgtgcc

14881 aggcatcatg ctaggcttgg gataaagctg tgactaagac accctcatcc tcatacagct

14941 tacattctag aagcagagac aaactggtga ataatagact ggtatattct acaaggcaaa

15001 accaaaaact gggcgcagta atgagaagaa taggggaacc cgctgtgcat caggtggttg

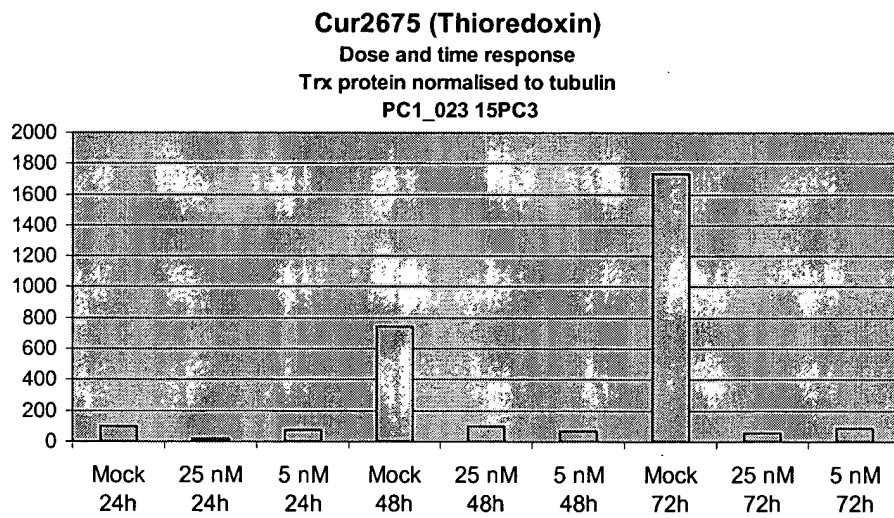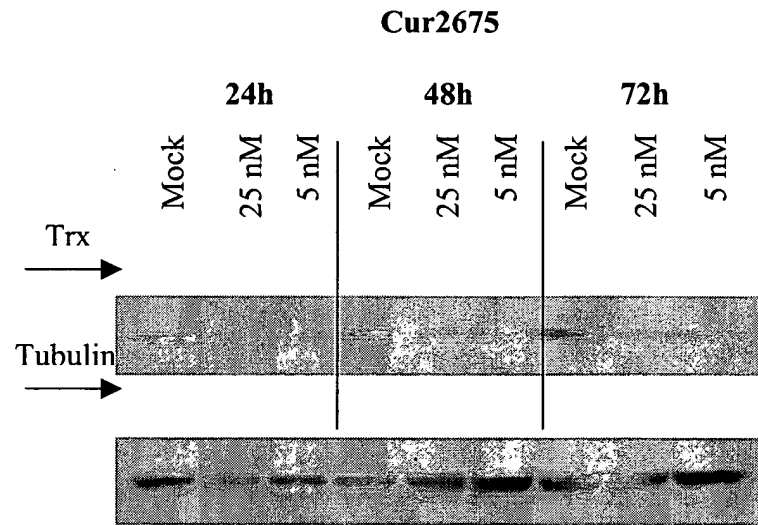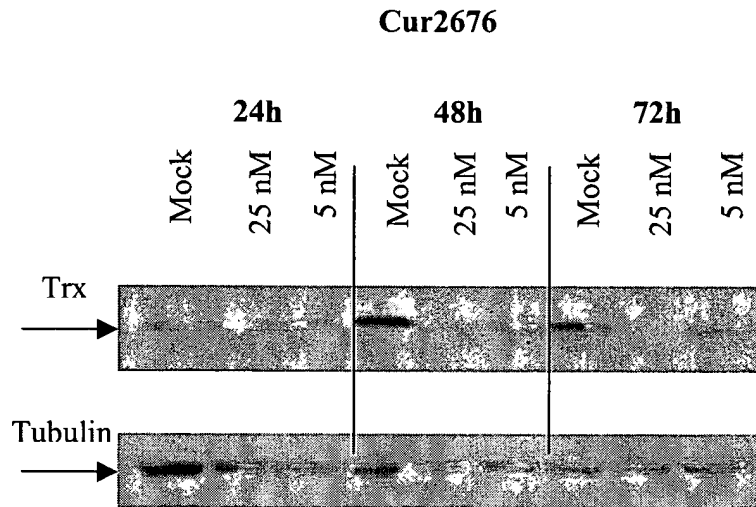15061 gacctgggtt ctttgaggtg actgtaaaca gagctgttgg

Figure 6/10

Cur2675

24h   **48h**   **72h**

Mock 25 nM 5 nM   Mock 25 nM 5 nM   Mock 25 nM 5 nM

Trx →

Tubulin →

Cur2675 (Thioredoxin)
Dose and time response
Trx protein normalised to tubulin
PC1_023 15PC3

| Mock | 25 nM | 5 nM | Mock | 25 nM | 5 nM | Mock | 25 nM | 5 nM |
| 24h | 24h | 24h | 48h | 48h | 48h | 72h | 72h | 72h |

Figure 7/10

Cur2676

Cur2676 (Thioredoxin)
Dose and time-response
Trx protein normalised to tubulin
PC1_023 15PC3

Figure 8/10

Sp cificity
Target cross r activity
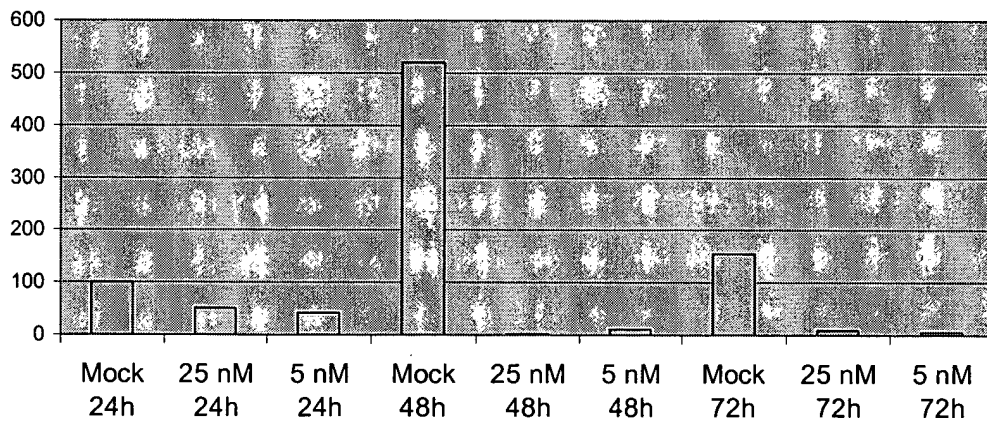**15PC3**

Figure 9/10
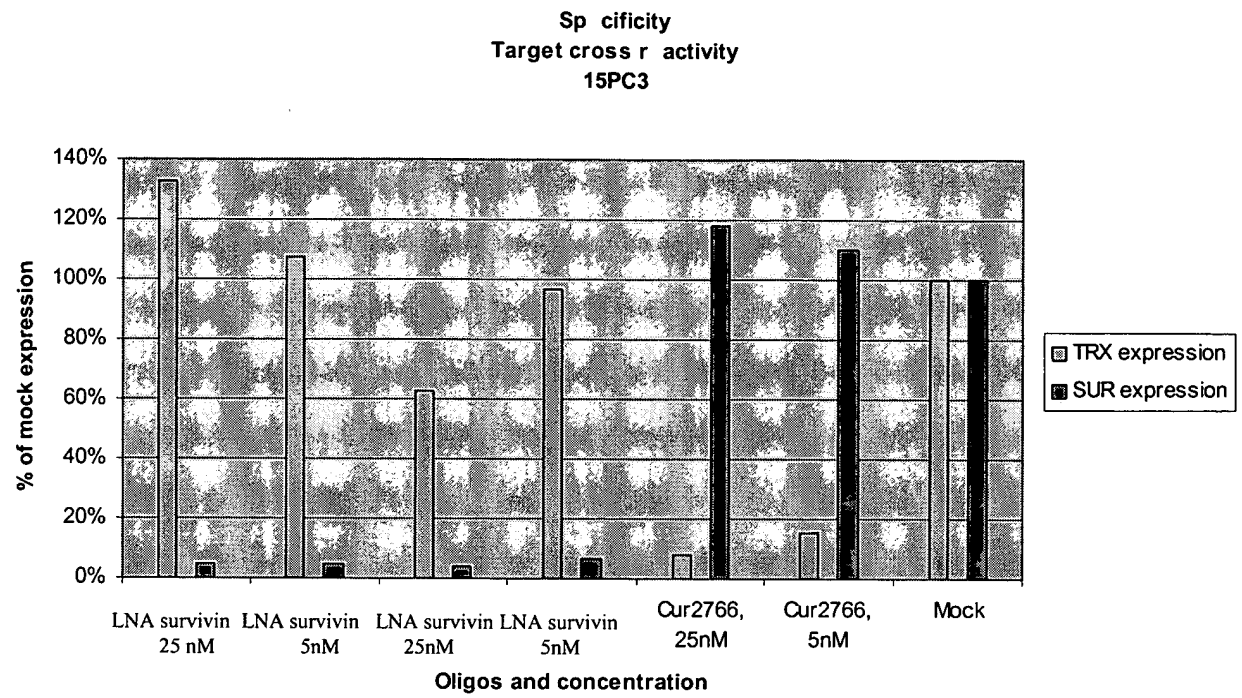

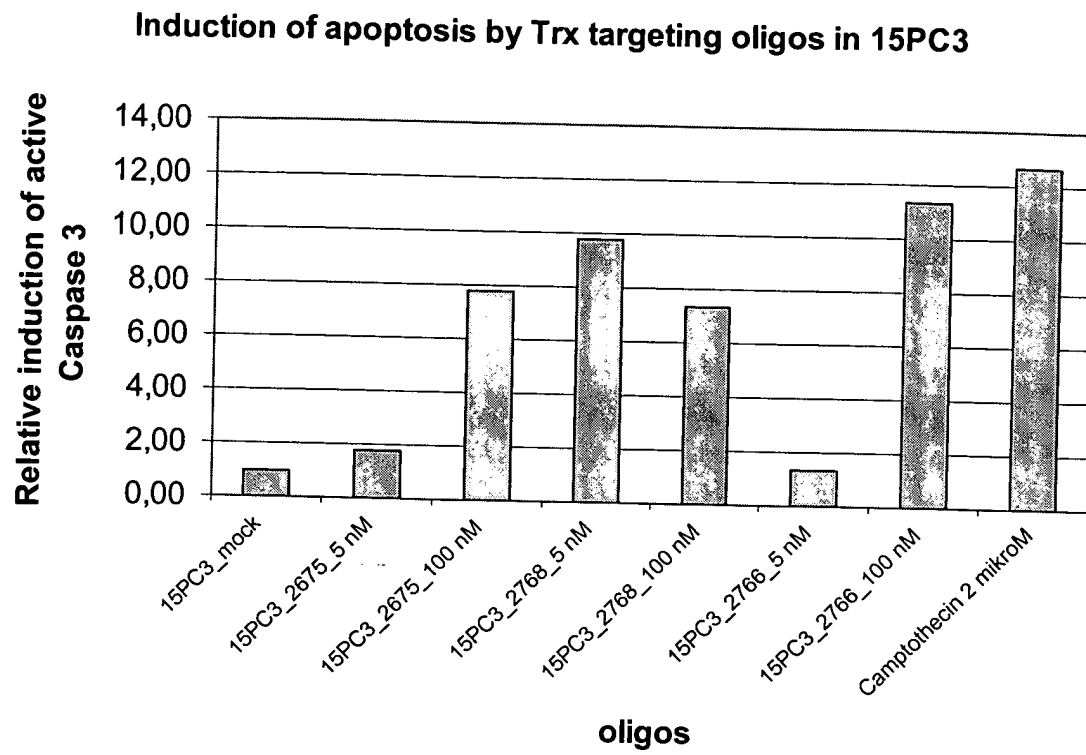Induction of apoptosis by Trx targeting oligos in 15PC3

Figure 10/10

Tumour growth
Thioredoxin antisense oligonucleotides s.c. day 7-20
HT29 colon cancer, BALB/c female nude mice
PD-03-053